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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/802,332	03/16/2004	Naoki Kimura	14875-040003/C1-806PCT-US	3754

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EXAMINER	
BELYAVSKYI, MICHAIL A	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 04/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/802,332	KIMURA ET AL.	
	Examiner	Art Unit	
	Michail A. Belyavskyi	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 February 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28-30 and 41-48* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *29* is/are allowed.

6)☒ Claim(s) *28,30 and 41-47* is/are rejected.

7)☒ Claim(s) *48* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANT'S AMENDMENT

1. Applicant's amendment, filed 02/28/06 is acknowledged.

Claims 28-30 and 41-48 are pending.

Claims 28-30 and 41-48 reads on an antibody that specifically binds to a polypeptide having at least 95 % identity to SEQ ID NO:2 are under consideration in the instant application.

In view of the amendment, filed 02/28/06 the following rejections remain

2. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 28, 30 and 41-46 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated antibody that specifically binds to a polypeptide consisting of SEQ ID NO:2 does not reasonably provide enablement for: (i) an antibody that specifically binds to a polypeptide having an amino acid sequence at least 90, 95 or 99 % identical to SEQ ID NO:2, claimed in claims 28; 41 and 42 or (ii) an antibody that specifically binds to a polypeptide encoded by the first nucleic acid that hybridized under stringent conditions to a second nucleic acid consisting of SEQ ID NO:3, recited in claim 30; (iii) an antibody that specifically binds to a polypeptide the amino acid sequence of which consists of SEQ ID NO:2 containing up to 30,15 5 or 3 amino acid substitutions, claimed in claims 43-46 . The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims for the same reasons set forth in the previous Office Action, mailed on 08/29/05.

Applicant's arguments, filed 02/28/06 have been fully considered, but have not been found convincing.

Applicant asserts that : (i) amended claims and new claims are analogous to those granted in U.S. Patent 6,784,284; (ii)Applicant provide ample guidance regarding the structure and function of the 7F4 protein and the changes and modification that can be made to the protein while retaining function.; (iii) the knowledge and skill in the art for producing the claimed polypeptide is high.

With regards to the issue that "amended claims and new claims are analogous to those granted in U.S. Patent 6,784,284"

It is well settled that whether similar claims have been allowed to others is immaterial. See In re Giolito, 530 F.2d 397, 188 USPQ 645 (CCPA 1976) and Ex parte Balzarini 21 USPQ2d 1892, 1897 (BPAI 1991). Moreover, as stated In re Borkowski, 505 F2d 713,718,184 USPQ29,33 (CCPA 1974), "The Paten Office must have the flexibility to reconside and correct prior decisions that may find to have been in error". In a similar context, the court in Fessenden v.Coe, 38 USPQ 516,521 (CADC 1938) stated that '[t]wo wrongs cannot make a right."

With regards to the issue that "Applicant provide ample guidance regarding the structure and function of the 7F4 protein and the changes and modification that can be made to the protein while retaining function.; and the knowledge and skill in the art for producing the claimed polypeptide is high.

Contrary to Applicant's assertion, as has been stated in the previous Office Action, Applicant disclosed a novel secretory protein 7F4 of SEQ ID NO:2, encoded by a nucleic acid of SEQ ID NO:3 that can induces differentiation of an osteocyte (see entire Specification, page 3, lines 15-30 and page 6, lines 15-30 in particular). Applicant also disclosed antibody that specifically binds said polypeptide consisting of SEQ ID NO:2 that can be used for purification, detection of said protein or for antibody therapy of bone disorder(see overlapping pages 14 –15). Applicant has not taught how to make and/or use (i) an antibody that specifically binds to a polypeptide having an amino acid sequence at least 90, 95 or 99 % identical to SEQ ID NO:2, claimed in claims 28; 41 and 42 or (ii) an antibody that specifically binds to a polypeptide encoded by the first nucleic acid that hybridized under stringent conditions to a second nucleic acid consisting of SEQ ID NO:3, recited in claim 30; (iii) an antibody that specifically binds to a polypeptide the amino acid sequence of which consists of SEQ ID NO:2 containing up to 30,15 5 or 3 amino acid substitutions, claimed in claims 43-46. The structural and functional characteristics of said polypeptides are not defined in the claim. Applicant has not provided sufficient biochemical information (e.g. structural characteristics, amino acid composition , physicochemical properties, etc) that distinctly identifies *any* polypeptide having an amino acid sequence at least 90 95 or 99 % identical to SEQ ID NO:2, or *any* polypeptide encoded by the first nucleic acid that hybridized under stringent conditions to a second nucleic acid consisting of SEQ ID NO:3, other than a polypeptide consisting of SEQ ID NO:2 or a polypeptide the amino acid sequence of which consists of SEQ ID NO:2 containing up to 30, 15, 5 or 3 amino acid substitutions that are capable to induces differentiation of an osteocyte. While any "polypeptide having an amino acid sequence at least 90, 95 or 99 % identical to SEQ ID NO:2, or *any* polypeptide encoded by the first nucleic acid that hybridized under stringent conditions to a second nucleic acid consisting of SEQ ID NO:3 or a polypeptide the amino acid sequence of which consists of SEQ ID NO:2 containing up to 30,15 5 or 3 amino acid substitutions " may have some notion of the activity of the " 7F4 protein of SEQ ID NO:2", claiming biochemical molecules by such properties fails to provide sufficient guidance and direction as to how the skilled artisan can make and use such antigens, to prepare antibody that can be used for purification and detection

7F4 protein of SEQ ID NO:2 or for antibody therapy of bone disorder commensurate in scope with the claimed invention.

Colman *et al.,* in Research in Immunology (145(1):33-36, 1994) teach single amino acid changes in an antigen can effectively abolish antibody antigen binding. Abaza *et al.,* in Journal of Protein Chemistry (11(5):433-444, 1992) teach that single amino acid substitutions outside the antigenic site on a protein effect antibody binding. Further, Lederman *et al* in Molecular Immunology (28:1171-1181, 1991) disclose that a single amino acid substitution in a common allele ablates binding of a monoclonal antibody (see entire document). Li *et al* in PNAS (77:3211-3214, 1980) disclose that dissociation of immunoreactivity from other biological activities when constructing analogs (see entire document). Moreover, Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Moreover, Whisstock et al (Quarterly Review of Biophysics, 2003, 36, pp307-340) teaches that prediction of protein function from sequence and structure is difficult problem, because homologous proteins often have different function. A fundamental problem is that function is in many cases an ill-defined concept (see Abstract in particular). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Finally, even single amino acid differences can result in drastically altered functions between two proteins. For example, Metzler et al. (Nature Structural Biol. 1997; 4:527-531) show that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 and CD86 (e.g., summarized in Table 2). Thus it is unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences.

In view of this unpredictability; the skilled artisan would not reasonably expect a polypeptide having anything less than 100% identity *over the full length of SEQ ID NO:2* to *share the same function* as the polypeptide of SEQ ID NO:2. Thus the recitation of percent identity language does not allow the skilled artisan to make and use *any* polypeptide having an amino acid sequence at least 90 95 or 99 % identical to SEQ ID NO:2, or *any* polypeptide encoded by the first nucleic acid that hybridized under stringent conditions to a second nucleic acid consisting of SEQ ID NO:3, other than a polypeptide consisting of SEQ ID NO:2 or a polypeptide the amino acid sequence of which consists of SEQ ID NO:2 containing up to 30, 15, 5 or 3 amino acid substitutions that can be used for purification and detection 7F4 protein of SEQ ID NO:2 or for antibody therapy of bone disorder commensurate in scope with the claimed invention without undue experimentation.

B. Similarly, the fact that two nucleic acid sequences will hybridize under moderate or stringent conditions does not in and of itself require that the two sequences share any functional activity. Thus the same observations apply to the recitation of "a polypeptide encoded by the first nucleic acid that hybridized under stringent conditions to a second nucleic acid consisting of SEQ ID NO:3" recited in claim 30 as were noted above with respect to "percent identity" language. Further, it was well known in the art at the time the invention was made that hybridization could occur between two sequence based upon short stretches of 100% identity. Thus a great deal of sequence variability *with respect to the full-length nucleic acid* is possible and in the absence of a clear recitation that the identity is over the full length of SEQ ID NO:3, the claim reads on subsequences and would be viewed by the skilled artisan as been even less likely to encode a polypeptide with the same function as polypeptide encoded by SEQ ID NO:2. Thus as for the recitation of percent identity, hybridization language in the absence of limitations regarding the *sequence length over which the hybridization takes place*; does not allow the skilled artisan to make and use any antibody that specifically binds to a polypeptide encoded by the first nucleic acid that hybridized under stringent conditions to a second nucleic acid consisting of SEQ ID NO:3, recited in claim 30 for purification and detection 7F4 protein of SEQ ID NO:2 or for antibody therapy of bone disorder commensurate in scope with the instant claims without undue experimentation.

Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use claimed (i) an antibody that specifically binds to a polypeptide having an amino acid sequence at least 90, 95 or 99 % identical to SEQ ID NO:2, claimed in claims 28; 41 and 42 or (ii) an antibody that specifically binds to a polypeptide encoded by the first nucleic acid that hybridized under stringent conditions to a second nucleic acid consisting of SEQ ID NO:3, recited in claim 30; (iii) an antibody that specifically binds to a polypeptide the amino acid sequence of which consists of SEQ ID NO:2 containing up to 30,15 5 or 3 amino acid substitutions, claimed in claims 43-46 in manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. *In re Fisher*, 166 USPQ 18(CCPA 1970) indicates that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute.

In view of the quantity of experimentation necessary, the unpredictability of the art, the lack of sufficient guidance in the specification, the limited working examples, and the limited amount of direction provided given the breadth of the claims, it would take undue trials and errors to practice the claimed invention.

The following new ground of objection and rejection are necessitated by the amendment filed 02/28/06.

4. Claims 44-46 are objected to as being in improper dependent form because claim 44 can not depend on itself.

Appropriate correction is required.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claim 47 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a New Matter rejection**.

" An isolated antibody that specifically binds to the extracellular region of 7F4 (SEQ ID NO:14) claimed in claim 47 represent a departure from the specification and the claims as originally filed and applicant has not pointed out where the support come from.

The specification and the claims as originally field only support for " An isolated antibody that specifically binds to a polypeptide consisting of SEQ ID NO:2.

7. The prior art does not teach or suggest the claimed invention recited in claim 29 and 48

8. Claim 48 is objected to as being dependent upon a rejected base claim 30, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

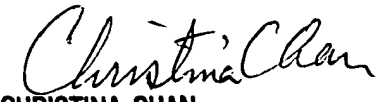
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is 571/ 272-0840 The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571/ 272-0841 .

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
March 31, 2006



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